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EFFECT OF BURN TRAUMA AND TOTAL-BODY IRRADIATION

- USSR -

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BIOCHEMICAL SHIFTS IN SHOCK PRODUCED BY THE COMBINED
EFFECT OF BURN TRAUMA AND TOTAL-BODY IRRADIATION

By D. A. Golubentsev and N. A. Shevyreva (Moscow)

[Following is the translation of an article by D. A. Golubentsev and N. A. Shevyreva in Patolog. Fiziol. i Eksper. Terapiya (Pathological Physiology and Experimental Therapy), Vol. IV, No 1, 1960, pages 14-19.]

The state of metabolism in combined radiation injuries has not been studied very much. Only scattered works have been devoted to the investigation of the various aspects of this important problem (10, 12, 17).

The principal task of the present work consisted of an experimental study of the carbohydrate metabolism in shock caused by the combined effect of burn trauma and total-body irradiation. Indices of the state of carbohydrate metabolism were the concentration of sugar, lactic acid and inorganic phosphate in the blood of dogs and the quantity of glycogen in rat tissues various intervals after the infliction of combined radiation injuries. In various series of experiments changes were investigated in the same biochemical indices of blood and tissues following the infliction of burn trauma alone or following total-body irradiation alone.

The objects of the investigation were mongrel dogs weighing from 11 to 18 kilograms and male white rats weighing from 160 to 250 grams.

Second- to third-degree burns were inflicted on dogs, using overheated steam on a shaved area of skin on the abdomen, chest and left thigh over an area which constituted 15-17 percent of the total body surface and with an

Exposure time of 10-15 minutes. The method of inflicting the burn in the dogs was described in detail in the work of V. N. Zhizhin and P. Ya. Mis'yukovich (6).

The combined radiation in dogs was associated with a total-body gamma-irradiation from a cobalt source (Co^{60}) with doses of 100, 200 and 400 r and second- to third-degree burns on the same area (15-17 percent). No more than 30 minutes elapsed between the conclusion of the irradiation and the infliction of the burn. The following were the conditions of irradiation: The dose rate in air was 502 r per hour; the distance, 110 centimeters.

Control data on the investigated biochemical blood indices in acute radiation injuries were obtained in dogs exposed to a total-body irradiation with 400-800 r. These animals died from acute radiation sickness seven-21 days after the irradiation.

During the first few hours after the irradiation signs of a primary early reaction were noted in the dogs: depression, loss of motor activity, sometimes a single or repeated vomiting. The blood pressure did not change essentially.

During the first few hours after the burn trauma or the combined effect in the dogs a shock state developed, as a rule, which was characterized by a reduction in the arterial pressure by 30 percent or lower, a rapid pulse with poor filling and low tension, shortness of breath, weakening or disappearance of the unconditioned reflexes (pupillary, corneal, pain), a reduction in body temperature and hemoconcentration. The rats were subjected to a total-body X-irradiation with 700 r under the following conditions: a "Stabilivolt" apparatus was used with a voltage of 160 kv, current 5 ma, filter 2.5 mm Al, half-value layer 0.28 mm of Cu, dose rate in air 28 r per minute, distance from the anode to the body surface of the animal, 70 centimeters. After the irradiation about 80 percent of the rats died from acute radiation sickness in eight to 30 days.

Third-degree burns were inflicted on the rats in the area of the back and lateral surfaces of the trunk using boiling water and an exposure time of five seconds. The area of the burn comprised 14-19 percent of the total body surface. When the rats were immersed in boiling water a marked motor reaction was observed. As early as the first few minutes after extraction from the water a shock state developed which was characterized by an almost complete

absence of voluntary motor activity, a weakening of the defense reflexes, a lowering of body temperature to 33-35°, hemoconcentration (hemoglobin content in the blood rose to 16-20 grams percent with a normal of 12-14 grams percent; the blood was viscous and dark in color). Part of the rats died from shock during the first few hours after the burn trauma or the combined effect. At later periods of time none of the rats died (30-day observation). The majority of the rats exposed to the combined effect died in five days; only in individual cases did the animals live up to 10 days.

The sugar content in the blood of the dogs was determined by Hagedorn-Jensen method; the lactic acid, according to the Friedemann, Cotonio and Schaeffer method; the inorganic phosphate, by the Fiske-Subbarow method. The glycogen content in the rat tissues was determined by the method of Good, Cramer and Somogyi.

The numerical data were treated statistically. The following were computed: the arithmetic mean (M), the average error of the arithmetic mean (m), the square root of the total of squares of the average errors (m_{diff}). The changes were considered reliable if the difference between the arithmetic means being compared exceeded the m_{diff} by two or three times. During the first few hours and days following the total-body irradiation of dogs with 400-800 r the content of sugar, lactic acid and inorganic phosphate in the blood did not undergo any regular considerable changes (Table 1).

Table 1

Content of Sugar, Lactic Acid and Inorganic Phosphate in the Blood of Dogs During the First Few Hours After a Total-Body Irradiation with 400, 600 and 800 r

Blood Index Studied	Dose of Radiation (r)	No. of Dogs	Content in Blood (mg%)				
			Before Irradiation	Time After Irradiation in Hours			
				1	2	4	6
Sugar	400	9	91 (78-102)	96 (80-104)	92 (76-106)	83 (78-92)	82 (78-88)
	600	8	89 (80-102)	92 (82-102)	90 (78-101)	92 (85-103)	83 (76-89)
	800	6	92 (76-108)	95 (82-110)	95 (83-103)	93 (79-105)	80 (79-84)
Lactic acid	400	7	14.4 (11-19)	—	16.8 (15-19)	14.0 (11-18)	12.3 (11-15)
	600	5	16.6 (10-20)	—	17.8 (16-20)	17.0 (14-21)	16.8 (12-21)
Inorganic phosphate	400	4	3.8 (3.2-4.4)	—	3.9 (2.9-4.3)	—	3.1 (2.8-3.3)
	600	5	4.5 (3.7-4.9)	—	4.1 (3.7-4.8)	—	3.6 (3.1-4.3)

Note: The figures within parentheses indicate the limits of variation in the content of the corresponding blood component.

These data are in agreement with the results obtained by other investigators (3, 4, 15, 20).

The combined effect of burn trauma and total-body irradiation with 100-400 r led to considerable changes in the content of sugar, lactic acid and inorganic phosphate in the blood of the dogs (Table 2).

Table 2

The Change in the Content of Sugar, Lactic Acid and Inorganic Phosphate in the Blood of Dogs in the First Few Hours After the Combined Effect of Burn Trauma and Total-Body Irradiation (100-400 r).

Degree of Severity of Shock	Blood Index Studied	No. of Dogs	Before the Effect	Content in Blood (mg%)			
				15 min.	1½ hours	3 hours	6 hours
Severe shock (death 3-3½ hrs. after the effect)	Sugar	4	92 (79-130)	169 (152-195)	61 (48-76)	65 (63-68)	--
	Lactic acid	4	15.5 (13-19)	64.8 (56-79)	44.0 (43-45)	36.7 (17-67)	--
	Inorganic phosphate	4	2.4 (2.1-2.7)	3.4 (2.7--4.0)	--	5.2 (4.7-5.8)	--
Non-fatal shock (survived for 24 hrs.)	Sugar	6	101 (90-125)	119 (96-198)	77 (63-112)	88 (60-102)	85 (56-106)
	Lactic acid	5	20.2 (12-26)	42.0 (39-48)	33.3 (11-63)	33.3 (11-77)	22.0 (12-30)
	Inorganic phosphate	5	2.1 (1.1-2.7)	1.7 (1.1-2.1)	2.0 (1.1-2.2)	2.3 (1.9-3.5)	4.0 (2.7-510)

Note: The figures within the parentheses indicate the limits of variations in the content of the corresponding blood component.

In four dogs during the first few minutes after the combined effect a severe shock developed with a fatal outcome after three-three and a half hours, and in six dogs, a less severe non-fatal shock. Fifteen minutes after the effect a pronounced although brief hyperglycemic reaction was observed in the dogs with the severe shock. As early as one and a half hours later the blood sugar content fell to hypoglycemic values and remained markedly reduced during the next few hours before the advent of death. With a non-fatal shock the initial hyperglycemic reaction and the subsequent hypoglycemic reaction were much less pronounced.

The content of lactic acid in the blood of dogs increased considerably as early as 15 minutes after the combined effect of burn trauma and total-body irradiation and remained high during the next few hours (determinations after one and one-half, three and six hours). The strength and duration of the hyperlactacidemic reaction depended on the rapidity of the development and degree of severity of the shock state. The content of inorganic phosphate in the development of non-fatal shock did not change essentially 15 minutes, one and one-half and three hours afterwards and increased six hours after the trauma. Fatal shock was characterized by the earlier and more considerable rise in the inorganic phosphate in the blood.

Experiments on rats showed that total-body irradiation with a dose causing the death of 80 percent of the animals during the second and third week after the irradiation did not lead to any considerable reduction in the glycogen level in the liver, myocardium, diaphragmatic and skeletal muscles during the first day (Table 3).

Table 3

Change in the Glycogen Content in the Rat Tissues Following Total-Body Irradiation, Burn Trauma or the Combined Effect of Burn Trauma and Total-Body Irradiation
(Average Data)

Nature of the Effect	Time After Effect (hrs.)	No. of Rats	Glycogen Content			
			Liver (g%)	Skeletal Muscle (mg%)	Diaphragm (mg%)	Myocardium (mg%)
			M ± m	M ± m	M ± m	M ± m
Control Irradiation	2	20	2.7 ± 0.2	512 ± 25	132 ± 11	403 ± 26
	4	10	2.4 ± 0.2	534 ± 31	446 ± 52	522 ± 26
	24	10	2.1 ± 0.1	519 ± 27	422 ± 18	492 ± 23
	48	10	2.7 ± 0.2	512 ± 32	413 ± 36	516 ± 35
	72	9	2.3 ± 0.2	492 ± 24	420 ± 39	490 ± 29
			1.8 ± 0.3	431 ± 32	351 ± 18	450 ± 18
Burn	2	4	0.4 ± 0.04	172 ± 12	115 ± 16	362 ± 22
	4	2	0.1 ± 0.01	193 ± 15	152 ± 17	321 ± 21
	24	4	0.1 ± 0.01	331 ± 19	312 ± 24	350 ± 18
	48	2	1.5 ± 0.1	326 ± 23	268 ± 25	282 ± 15
	72	4	1.2 ± 0.1	412 ± 31	510 ± 31	400 ± 24
Combined effect	2	4	1.1 ± 0.1	241 ± 22	191 ± 15	370 ± 23
	4	10	0.1 ± 0.01	211 ± 19	172 ± 19	402 ± 18
	24	15	1.8 ± 0.1	370 ± 26	319 ± 29	330 ± 19
	48	10	1.3 ± 0.1	295 ± 21	263 ± 23	208 ± 22
	72	20	0.9 ± 0.05	332 ± 22	322 ± 19	321 ± 19

The burn trauma without irradiation or in combination with total-body irradiation produced almost a complete decomposition of the glycogen in the liver, a marked reduction in its level in the skeletal muscles and diaphragm.

(on the average, by 2.1-3.7 times) and a moderate reduction of it in the myocardium as early as two to four hours after the trauma. During the course of the next three days the content of glycogen increased somewhat in the liver, skeletal muscles and diaphragm of the burned animals and the rats which had been subjected to combined injuries, and remained considerably below normal. In the myocardium a further reduction occurred in the glycogen content, which was expressed more markedly in the case of combined injury.

The data presented showed that the following were the characteristic biochemical changes in shock developing in dogs and rats following the combined effect of burn trauma and total-body irradiation: a rapid breakdown of the glycogen reserves of the organism, the accumulation of lactic acid and inorganic phosphate in the blood, a brief hyperglycemic reaction, subsequently replaced by a persistent decrease in the sugar content in the blood to hypoglycemic levels.

The rapidity of development, strength and duration of the hyperlactacidemic, hypoglycemic and hyperphosphatemic reactions were directly related to the rapidity of development and the degree of severity of the shock state.

A comparison of the changes in carbohydrate metabolism produced by a total-body irradiation and burn trauma leads to the conclusion that the chief role in the occurrence of these changes with the combined effect of a burn and irradiation during the first few hours is played by the burn trauma. However, the combination of burn trauma with radiation trauma leads to certain qualitative changes in the nature of the metabolic disturbances.

The metabolic changes in burn shock are analyzed in detail in the review of I. R. Petrov (14) and the monograph of B. N. Postnikov (16). The authors point out that a persistent hyperglycemia is characteristic of burn shock in people and laboratory animals. During the first few hours and days after the burn trauma many research workers found a hyperglycemia (1, 2, 7, 8, 9, 11, 13). Thus, according to the data of G. F. Milyushkevich (11), obtained on 390 patients, during the first few days after the burn trauma a hyperglycemia is noted which develops, as a rule, in patients with extensive burns; hypoglycemia occurred only in the second week of the burn sickness. Similar results were obtained by other research workers. We observed a reduction in the sugar content in the blood as early as the first few hours in dogs exposed to the combined effect of burn

trauma and total-body irradiation. This reduction is evidence, probably, of the early inadequacy of the carbohydrate function of the liver following a burn-radiation trauma. In hypoglycemia the carbohydrate supply of the tissues is reduced and, particularly, that of the central nervous system, which may exert an unfavorable influence on the course of the pathological process. Therefore, the hypoglycemia should be prevented or lessened. The data presented in our work constitute the experimental basis for the study of the role of glucose therapy in combatting shock caused by the combined effect of burn and radiation trauma. Naturally, glucose therapy should be only a component part of the total comprehensive therapy of the shock state and should be used only in the event the glucose administered is assimilated. This problem will be discussed by us in the next report.

Glucose therapy is being widely used in the treatment of burn sickness, chiefly during the period of toxemia (8, 16).

On the basis of existing data in the literature the results of the present work may be interpreted in the following way. Burn and burn-radiation trauma, produce, evidently, a reduction of energy production needed for activity during the course of oxidative reactions during the first few hours. A reduction in the oxidative processes in burn and burn-radiation trauma may be determined by many factors. Among them an important role is played, evidently, by changes in the circulation and respiration (14) and, possibly, by a change in the quality of the oxidative processes (5). During the first few hours after the trauma the tissue oxygen requirement is higher than normal, and the possibility of obtaining it is less than normal (16). As a result of the reduction in the oxidative processes a tissue anoxia develops which produces a compensatory activation of anaerobic glycolysis and a consequently inevitable rapid consumption of glycogen reserves on the body. The anoxia also leads to an accumulation of insufficiently oxidized products in the blood.

The hyperglycemia which develops is, in our opinion, a compensatory reaction of the body, directed toward the maintenance of a definite level of carbohydrate supply for the vital organs; the hypoglycemia, apparently, attests to the occurrence of an insufficiency of the carbohydrate function of the liver and requires effective measures for its prevention.

Conclusions

1. The shock state which develops in dogs and rats during the first few hours after the combined effect of burn trauma and total-body external irradiation is characterized by the rapid depletion of the glycogen reserves of the body, the accumulation of lactic acid and inorganic phosphate in the blood, a brief hyperglycemic reaction which is then replaced by a persistent reduction in the blood sugar to hypoglycemic levels.

2. Total-body external irradiation even with a dose near the minimum absolutely lethal dose does not cause any such changes in carbohydrate metabolism during the first few hours or days.

3. Changes in the carbohydrate metabolism which are observed during the first few hours following the combined effect are determined chiefly by the burn trauma.

4. Total-body irradiation which is superimposed on the burn trauma leads to a more severe course of the pathological process, the earlier death of the animals and a disturbance of the compensatory metabolic reactions.

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